UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,116	01/26/2001	Howard Benjamin	PPI-012CN	9135

959 7590 03/19/2003

LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER
PONNALURI, PADMASHRI

ART UNIT	PAPER NUMBER
1639	9

DATE MAILED: 03/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/772,116	Benzamin et al
Examiner	**Art Unit**
Padmashri Ponnaluri	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 11, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above, claim(s) *24-34* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-23* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *2, 3*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election without traverse of group I, claims 1-23, in Paper No. 8, filed on 12/11/02, is acknowledged..

2. The preliminary amendment filed on 1/26/01, has been fully considered and entered into the application.

3. This application is a continuation of application 08/573,786, filed on 12/18/1995.

4. Applicants are requested to update the current status of parent application data in the specification page 1.

5. Claims 24-34 are withdrawn from further consideration pursuant to 37 CAR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 8.

6. Claims 1-23 are currently being examined in this application.

7. The disclosure is objected to because of the following informalities: the specification in page 6, line 37, the US Patent application No is left blank..

Appropriate correction is required.

8. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CAR 1.821(a)(1) and (a)(2). Applicants rely filed on 5/24/02 to the notice to comply with sequence compliance has been fully considered and entered. However, the sequences in page 12 and 14 fail to comply with the requirements of 37CFR 1.821 through 1.825. If applicants believe these sequences comply with the sequence rule

requirements, applicants are requested to amend the specification to include the Sequence identification numbers.

9.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims recite ' a method for identifying a compound that binds to a target and the method comprising ; a) forming a first library comprising a multiplicity of peptides; b) selecting from the library at least one peptide that binds to the target;....' Thus in the claimed method after step b) a compound (peptide) that binds to the target is already identified. Thus, it is not clear what does applicants mean by the reset of the method steps. Does applicants mean that the method is drawn for identifying a non-peptide compound that binds to a target? Applicants are requested to amend the claim.

Claims recite that the second library comprises 'non-peptide compounds'. The specification definition or explanation of 'non-peptide compounds' seem to be confusing. The specification discloses in page 2, that '.. **the non-peptide library comprises compounds that, while not peptides, are structurally related to peptides, such as peptide analogues, peptide derivatives and/or peptidomimetics**....' However, the term 'non-peptide' is vague because

according to the definition they are **not peptides**, but analogues of peptides or derivatives of peptides. It is not clear how the peptide analogues and derivatives are not peptides. Applicants are requested to clarify. The non-peptide' compounds in the instant claims are considered as compounds which do not have any natural and unnatural amino acids present in them. The small organic heterocyclci compounds or antibiotics would be considered as non-peptide compounds according to the instant claims or only peptide compounds with certain amino acids replaced by synthetic amino acids is considered as non peptides, it is not clear. If applicants mean that the non-peptide compounds are peptide compounds with certain amino acids replaced by synthetic amino acids, applicants are requested to clearly recite them as peptide compounds with unnatural amino acids.

Claim 4 recites that the first library is an anchor library. Applicants are requested to clarify what does applicants mean by anchor library? Does the anchor library different from the claim 3 library which is bound to a solid support.

Claim 8 is indefinite by reciting 'wherein step c) comprises determining the nucleotide sequence of nucleic acid molecule or molecules that encode at least one peptide. Claim 1 step c) recites method for determining the sequence of at least one peptide that binds to the target. It is not clear how determining the peptide sequence in step c) comprises determining nucleotide sequence. The method steps for determining the nucleotide sequence of the peptide is not same as the method steps for determining the peptide sequence. Applicants are requested to cancel the claim.

Claim 9 recites the limitation "the amino acid sequence" . There is insufficient antecedent basis for this limitation in the claim or in claim 1.

Claim 10 vague and indefinite by reciting 'second library comprises at least one peptide derivative.' Claim 1 in step d) recites that forming a second library comprising non-peptide compounds. Thus, it is not clear what does applicants mean in claim 10, peptide derivative. It is not clear what are the meets and bounds of the term 'derivative', does applicants mean modified peptides. Further the peptide derivatives do not include the non-peptide compounds of claim 1. Applicants are requested to clarify.

Claim 11 recites 'second library comprises peptide analogue', it is not clear what are the meets and bounds of the term 'peptide analogues', does applicants mean that the peptide analogues are different from peptide derivatives. Further it is not cleat how peptide analogues are not peptides. Claim 1 in step d) recites that forming a second library comprising non-peptide compounds. Thus, it is not clear what does applicants mean in claim 11, peptide analogue. Applicants are requested to clarify.

Claim 21 recites that 'forming a third library comprising a multiplicity of non-peptide compounds designed based on the structure of the non peptide compounds determined in step f)...' it is not clear how the third library of compounds are different from the second library of compounds. According to the claims the first library is peptide library, and the second library is non-peptide library, and it is not clear how the third library is different from the non-peptide

library of second library. Does applicants mean that the structure of the compound identified from second library is modified to derive a third library. Applicants are requested to clarify.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claim 21 briefly recites methods for forming a third library based on the selected non-peptide compounds identified from the second library.

The instant specification discloses methods of identifying a peptidomimetic which binds to a target. The specificating method discloses that a first peptide library is screened for binding of target, and using the identified compound a peptidomimetic or displacing some of the natural amino acids with synthetic amino acids a second library is formed. And the second library is screened for identifying compounds that bind to a target. The specification examples are drawn to a phage display library of peptides as a first library and replacing some of the amino acids of the identified compound which binds to the target from the first library with synthetic amino acids to prepare the second library, and methods of screening the second library for binding with the target.

The specification description is directed to specific peptide compounds which specifically bind to LHRH-R and modifying by replacing certain amino-acids in the identified peptide to generate second library which clearly do not provide an adequate representation regarding the method of generating the third library of compounds made by the presently claimed invention.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

In the present instance, the claimed invention contains no identifying characteristics regarding the third library of compounds. The specification examples do not recite the third library and how they are different from the second library.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 3-4, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirshmann et al (J. American chemical Society, vol. 114, No. 24, 1992, pages 9699-9701) and Blake (US Patent 5,565,325).

Hirshmann et al teach the synthesis of non-peptide libraries of peptidomimetic based upon known peptide ligand (motif). The reference teaches that the identification of the compounds from the library which bind to the target. As the synthetic paths of the compound since the library are known, Hirshmann et al are able to determine the structure of the non-peptide library members. Hirshmann et al do not specifically teach the formation of the first peptide library and identifying the peptide which binds to the target and determining the motif.

Blake teaches a method for screening for peptide library to identify peptides that bind to target receptors and to optimize ligand sequences by varying the residues at non-essential positions. Blake teaches that the peptide libraries can be made using Merrifield synthesis (solid support bound) methods.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to identify the peptide motif as taught by Blake and use the motif in the method of Hirshmann et al for identifying a non-peptide compound that binds to a target, since Hirshmann et al teaches that the structure of a known peptide motif can be used as the basis of a non-peptide library.

15. Claims 1, 3-7, 9-15, and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirshmann et al and Blake as applied to claims 1, 3-4 and 9-12 above, and further in view of Gordon et al (J. Medicinal Chemistry. Vol. 37, no. 10, 1385-1401, 1994).

Hirshmann et al and Blake have been discussed supra. The references do not teach the size of the first or second library. However, Gordon et al teaches that the libraries as large as 10^{12} members ans indicates that large libraries (10^{12} - 10^{6} compounds) are useful in lead identification and intermediate size libraries are useful in chemical analologing and small libraries (10^{2} or less are useful for fine tuning (i.e., see figure 1 and 19 and associated text). Gordon also teaches that eh libraries of peptido mimetics are known in the art (i.e., peptoids figure 4) which can be interpreted as peptide analogues and/or peptide derivatives. In addition the reference teaches that the

identification of compounds with modest or high affinity from the libraries is well known in the art.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to identify a motif as taught by Blake and use the motif in the synthesis of non-peptide compounds and identification of non-peptide compound which binds to a target as taught by Hirshmann et al. Furthermore, it would have been obvious to specifically make large libraries to identify lead compounds, and to identify compounds having specific affinity and to make additional libraries to fine tune as taught by Gordon et al in order to identify lead structures more effectively. One would have been motivated to make the large libraries as taught by Gordon et al such that additional fine tuning of the compounds can be made.

16. Claims 1, 3-4, 9-12, 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirshmann et al, Blake as applied to claims 1, 3-4, 9-12 above, and further in view of Stankova et al (Drug Development Research. vol. 33, pages 146-156, 1994).

Hirshmann et al and Blake have been discussed supra. The combined teachings of the references do not teach the use of mass spectroscopy or tandem mass spectroscopy. However, Stankova et al teaches the use of tandem mass spectroscopy for analysis of structure of compounds identified from a library.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to identify a motif as taught by Blake and use the motif in the synthesis of non-peptide compounds and identification of non-peptide compound which binds to a target as

taught by Hirshmann et al. Furthermore, it would have been obvious to specifically use tandem mass spectroscopy in analyzing the structure of the compounds identified from the library, since Stankova et al teach the use of tandem mass spectrometry in identifying the compound structure.

17. Claims 1, 3-4, 8-12 16-17 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirshmann et al, Blake et al, Stankova et al and further teachings of Scott et al (science, vol. 249, 386-390, 1990).

Hirshmann et al teach the synthesis of non-peptide libraries of peptidomimetic based upon known peptide ligand (motif). The reference teaches that the identification of the compounds from the library which bind to the target. As the synthetic paths of the compound since the library are known, Hirshmann et al are able to determine the structure of the non-peptide library members.

Blake teaches a method for screening for peptide library to identify peptides that bind to target receptors and to optimize ligand sequences by varying the residues at non-essential positions. Blake teaches that the peptide libraries can be made using Merrifield synthesis (solid support bound) methods.

Stankova et al teaches the use of tandem mass spectroscopy for analysis of structure of compounds identified from a library.

The combined teachings of Hirshmann et al, Blake and Stankova et al do not teach that the first library of compounds are anchored or displayed on the surface of bacteriophage. However, Scott et al teaches that the sequence of peptide ligands having affinity for a target molecule in phage display epitope library can be deduced by screening the library and then

determining sequence of the phage nucleic acid which encodes the peptides. Scott et al teach a hexapeptide library.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use phage display library taught by Scott et al as first library and identify a motif from the first library as taught by Blake and use the motif in the synthesis of non-peptide compounds and identification of non-peptide compound which binds to a target as taught by Hirshmann et al, and further use tandem mass spectroscopy in analyzing the structure of the compounds identified from the library, since Stankova et al teach the use of tandem mass spectrometry in identifying the compound structure.

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 U. S. P. Q. 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 U. S. P. Q. 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 U. S. P. Q. 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 U. S. P. Q. 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CAR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CAR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CAR 3.73(b).

19. Claims 1-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 12-20, 22-26, 41-53 of copending Application No. 08/769,250. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed methods are exactly same as the reference claim methods, except the reference recites that the second library comprises peptide analogues which may read on the non-peptide compounds of the instant second library compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Primary Examiner
Technology Center 1600
Art Unit 1639
19 March 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER